

## AMENDED CLAIMS

[received by the International Bureau on 28 January 2005 (28.01.05);  
original claim 1 amended, original claims 2 and 3 deleted, remaining claims renumbered but  
unchanged. (3 pages)]

1. A pharmaceutical composition for controlled drug delivery comprising a  
5 cephalosporin antibiotic and a combination of at least two carbomers.
2. The composition of claim 1 wherein said cephalosporin antibiotic is selected from  
cefdinir, cefditoren pivoxil, cefepime, cefixime, cefoperazone, cefotetan,  
cefpodoxime paroxetil, cefprozil, cefazidine, ceftibuten, ceftriaxone, cefuroxime  
axetil, cephalixin, cefaclor, cefadroxil, cefamandole, cefoxitin, cefalothin,  
10 moxalactum, cefapirin, ceftizoxime, cefonicid, cephradine, loracarbef, cefetamet  
and pharmaceutically acceptable hydrates, salts or esters thereof.
3. The composition of claim 2 wherein said cephalosporin is cefprozil or its  
pharmaceutical acceptable hydrates, salts or esters.
4. The composition of claim 3 wherein said cefprozil or their pharmaceutical  
15 acceptable hydrates, salts or esters may be present in an amount from 100 mg to  
1000 mg.
5. The composition of claim 3 wherein said cefprozil or their pharmaceutical  
acceptable hydrates, salts or ester may be present from about 30-90% w/w of the  
formulation.
- 20 6. The composition of claim 1 wherein said carbomers are a mixture of Carbopol  
971P® and Carbopol 974P®.
7. The composition of claim 1 wherein said carbomers comprise about 0.1% to 50%  
by weight of the controlled release composition.
8. The composition of claim 7 wherein said carbomers are present at a concentration  
25 from about 5 % to about 50 % comprising of Carbopol 971P in an amount from  
about 0.1 % to about 20 % by weight and Carbopol 974P in an amount from  
about 0.1% to about 30 % by weight of controlled release composition.
9. The composition of claim 1 which further comprises other pharmaceutically  
acceptable excipients selected amongst water-soluble or water dispersible diluents  
30 and lubricants.
10. The composition of claim 9 wherein said water-soluble diluent is selected from  
lactose, mannitol, glucose, sorbitol, maltose, dextrans, dextrans and the like.

11. The composition of claim 10 wherein said water-soluble diluent is lactose.
12. The composition of claim 11 wherein said lactose amounts from about 5% to about 20% by weight of the formulation.
13. The composition of claim 9 wherein said water dispersible diluent is selected  
5 from amongst microcrystalline cellulose, starch, pre-gelatinized starch, magnesium aluminum silicates and the like.
14. The composition of claim 13 wherein said water dispersible diluent is microcrystalline cellulose.
15. The composition of claim 14 wherein said microcrystalline cellulose amounts  
10 from about 5% to about 20% by weight of the formulation.
16. The composition of claim 9 wherein said pharmaceutical excipient is either one or a combination of lubricants at a concentration in the range of about 0.2% to 5% by weight of the composition.
17. The composition of claim 9 wherein said lubricant is selected from talc, stearic  
15 acid, magnesium stearate, colloidal silicon dioxide, calcium stearate, zinc stearate, hydrogenated vegetable oil and the like.
18. The composition of claim 17 wherein said lubricant is preferably selected from talc, stearic acid, magnesium stearate and colloidal silicon dioxide.
19. The process for the preparation of the pharmaceutical composition comprising  
20 mixing together, a cephalosporin antibiotic or their pharmaceutically acceptable hydrates, salts or esters; with combination of carbomers and optionally, with one or more water soluble or water dispersible diluents and lubricants to form the blend, and compressing the blend into tablets.
20. The process of claim 19 wherein the blend may be compacted into granules.
21. A controlled release composition of cephalosporin antibiotic comprising a  
25 pharmaceutically effective amount of cephalosporin antibiotic, combination of carbomers, a water-soluble and /or water dispersible diluent and pharmaceutically acceptable tablet excipients for controlling the release of cephalosporin antibiotic.
22. A controlled release composition comprising a cephalosporin antibiotic and a  
30 release controlling polymer wherein the  $C_{max}$  is substantially the same as that of a single dose of an immediate release formulation.

23. A controlled release composition of claim 22 wherein the cephalosporin antibiotic is cefprozil

5 24. A controlled release composition comprising a cephalosporin antibiotic and a release-controlling polymer wherein the  $T > MIC$  at 0.25 mcg/ml was achieved for about 75% of the dosing interval and  $T > MIC$  of 2 mcg/ml was achieved for almost 49% of the dosing interval.

25. A controlled release composition of claim 24 wherein the cephalosporin antibiotic is cefprozil.

10 26. A controlled release composition comprising from about 30- 90 % w/w of cefprozil and from about 0.1-50 % by weight of one or a mixture of carbomers and optionally one or more pharmaceutically acceptable excipients selected from amongst diluents and lubricants.

15 27. A controlled release composition of claim 26 preferably comprising from about 40-80%w/w of cefprozil and from about 0.1-40 % w/w of one or a mixture of carbomers and optionally one or more pharmaceutically acceptable excipients selected from amongst diluents and lubricants.

**STATEMENT UNDER ARTICLE 19**

The present invention relates to controlled release compositions of  $\beta$ -lactam antibiotic agent namely cephalosporins and at least two carbomers.

**XP 002278979** cited in the International Search Report as category citation teaches enteric-coated cefaclor micro granules prepared by extrusion and airflow coating method. This composition is suitable for twice daily administration and is delayed release type.

**US 3,074,852** also cited in the International Search Report teaches sustained release formulations utilizing a particular grade of carbopol-934. This polymer characteristically provides a zero order release profile of the active ingredient. However, for the cephalosporins, which are preferably absorbed from the proximal part of GIT, carbopol 934 would not be suitable.

In addition, the cited prior art defines drug to polymer ratio to be at least 1:0.5. Such ratio may not be applicable to the present invention, where the drug to polymer ratio is about 1:0.35.

The present application is directed towards use of at least two carbomers namely combination of Carbopol 971P and Carbopol 974P which produces a semi enteric effect, whereas Carbopol 974P, on the other hand, provides a prolonged linear release profile.

**US 3,639,560** cited in International Search Report discloses the invention, which is primarily applicable in the dry period therapy in the treatment and control of bovine mastitis. Column 3, line 4 discloses various therapeutic agents used in the above invention. Column 4, column 5, example 4 discloses dispersion of sustained release formulation in 0.5% w/v carbopol 934 aqueous vehicle.

In contrast to the above US patent '560, which defines intra-mammary injectable dosage form of active substance, the present formulation is for oral administration in the form of tablets.

Further, Carbopol is only a suspension aid in '560, whereas combination of carbomers namely carbopol 971P and 974P are used as release modifying agent in the present invention.

**WO 2004/019901** cited in the International Search Report under "E" category was published later than the filing of the present application and does not require comments.

As stated above, it is clear that none of the cited art alone or in combination teaches the present invention. There is no motivation in the cited art that controlled release type composition comprising cephalosporin and at least two defined carbomers may be formed. The present inventors have found that combination of the specified carbopols are capable for providing the control of the release of active ingredient. Taking cue from the cited art it would not be possible to combine the carbopol 971 and 974 along with cephalosporin to provide a pharmaceutical composition for controlled drug delivery wherein combination of the Carbopol 971P and Carbopol 974P can be manipulated to achieve the desired drug release profile suitable for the specific needs of cephalosporins. Further, the specific polymer to drug ratio of the present invention is also not taught or motivated from the cited art.

To emphasize the above distinguishing features the applicant wishes to amend the claims based on the description which may please be taken as amendment under Article 19.